Reference Materials for Genetic Testing

-

ISO Standardization

Klaus Stinshoff
Digene Switzerland Sarl

Definitions

Biological Standard (according to WHO):

Biological substance which cannot be completely characterized by physico-chemical means alone, and which therefore requires the use of some form of bioassay

NOTE: The underlying principle of such assays is that they depend on the comparison of the response of the test substance with that of a reference material.

(A.F.Bristow, Sevres, 2002 – modified)

Definitions

Standard (according to ISO):

Document, established by consensus and approved by a recognized body, that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context.

NOTE: Standards should be based on the consolidated results of science, technology and experience, and aimed at the promotion of optimum community benefits.

(ISO/IEC Directives, Part 2:2001)

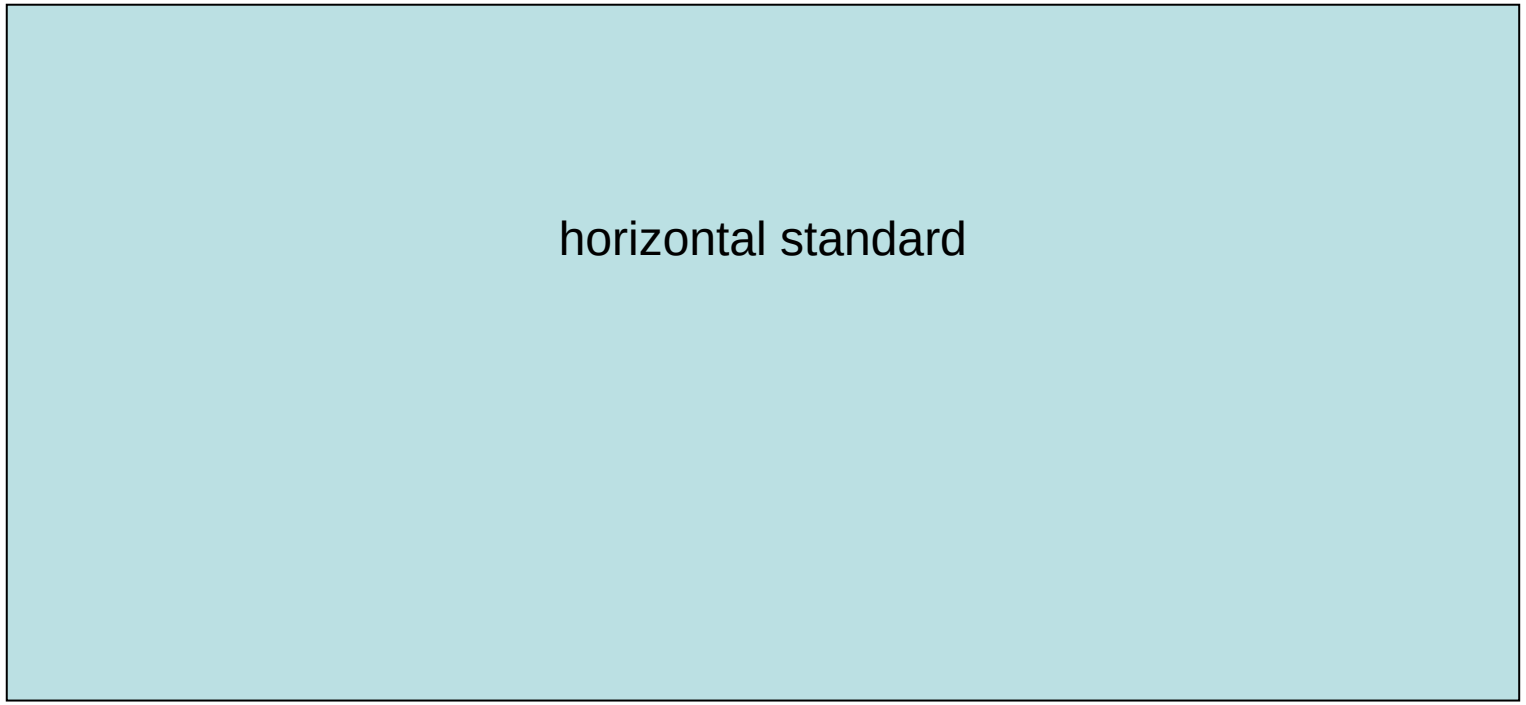
ISO Standardisation

Classes of Standards:

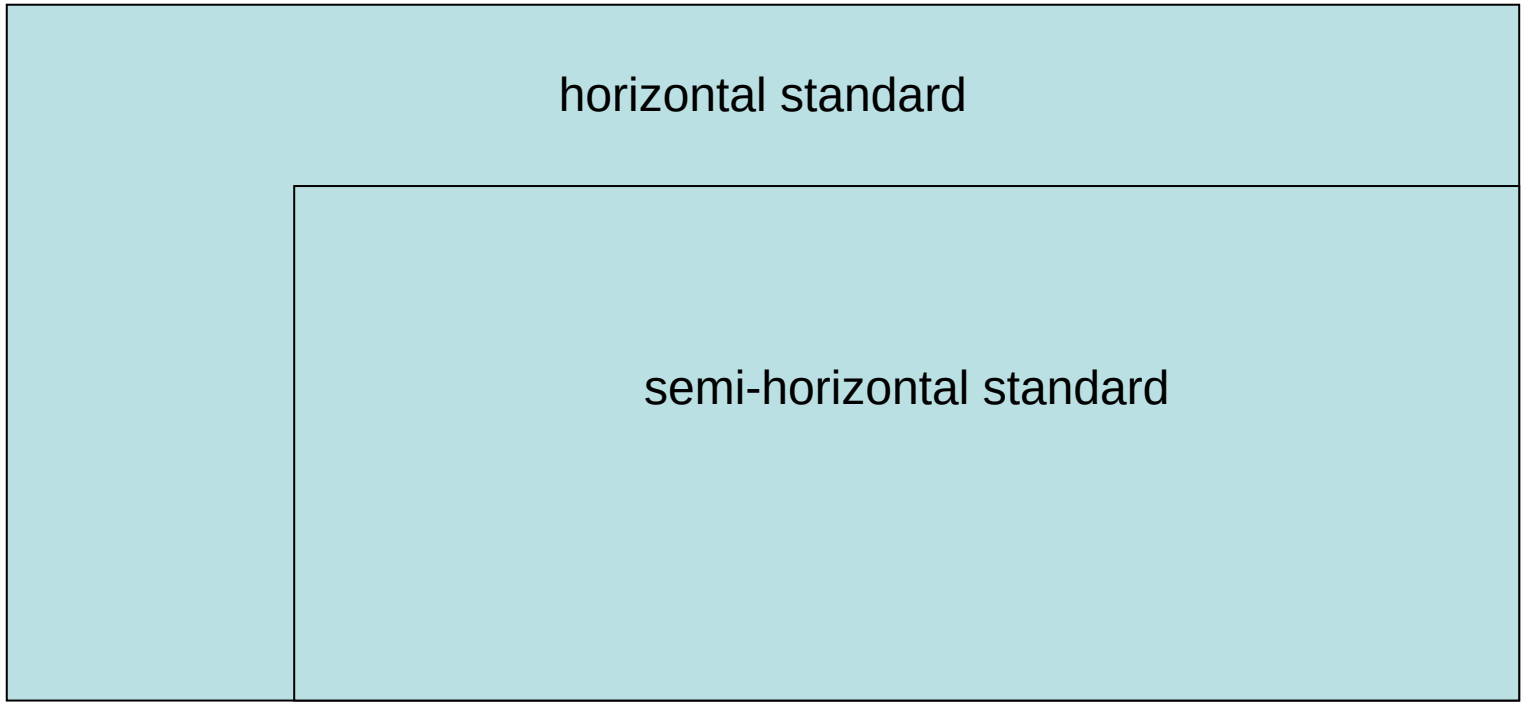
- **horizontal standards**: Standards indicating fundamental concepts, principles and requirements with regard to general aspects applicable to all kinds or a wide range of products and/or processes (e.g. ISO 17511:2003)
- **semi-horizontal standards**: Standards indicating aspects applicable to families of similar products and/or processes making reference as far as possible to horizontal standards (e.g. ISO 18153:2003) and
- **vertical standards**: Standards indicating necessary aspects of specific products and/or processes, making reference, as far as possible, to horizontal standards and semi-horizontal standards

(GHTF, SG1/N044R4, 2002)

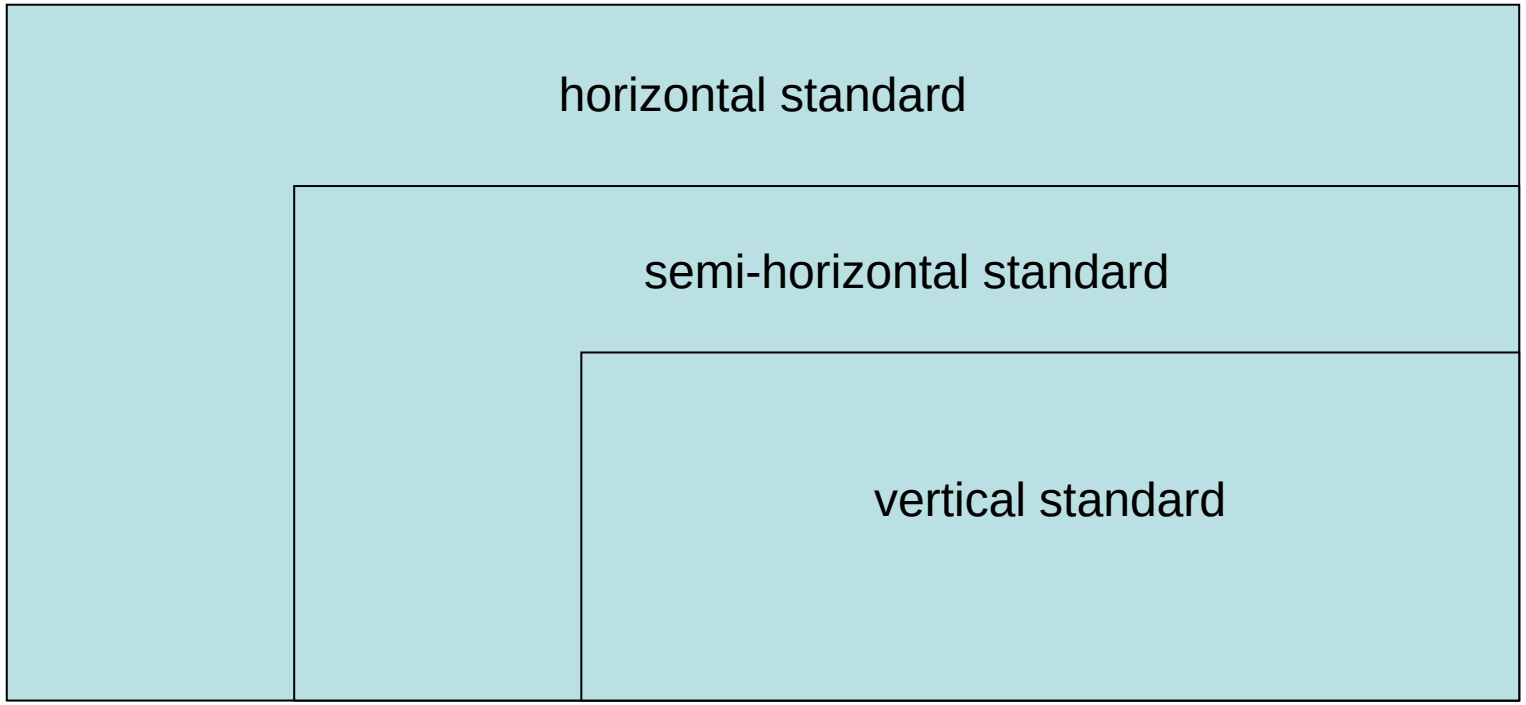
Classes of Standards



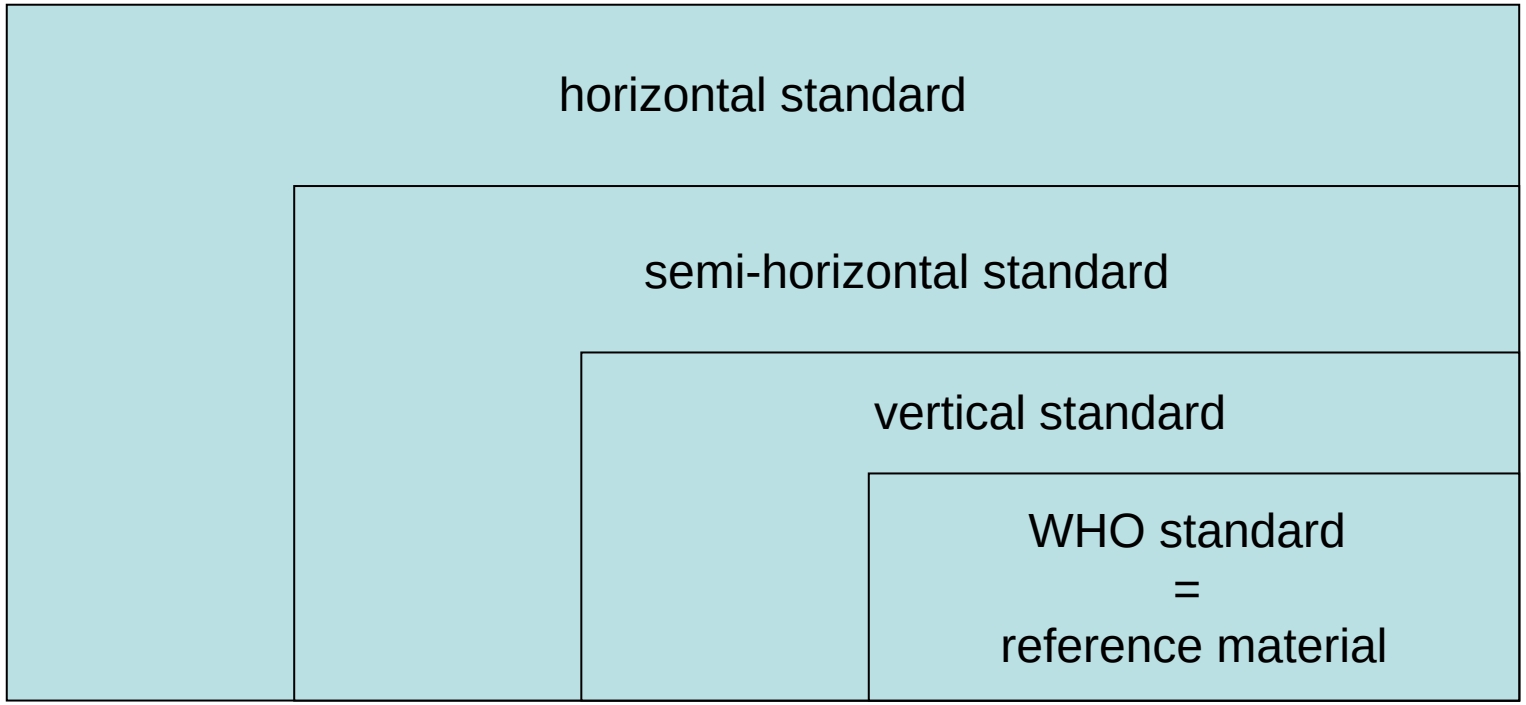
Classes of Standards



Classes of Standards



Classes of Standards



ISO Standardisation

Performance vs. Prescriptive Standards:

Whenever possible, requirements shall be expressed in terms of performance rather than design or descriptive characteristics. This approach leaves maximum freedom to technical development….

(Excerpt of Clause 4.2, ISO/IEC Directives, Part 2, 2004)

NOTE: This requirement is based on Annex 3 of the WTO Agreement on Technical Barriers to Trade, 2000.

ISO/TC 212

ISO/TC 212 Strategies:

- Select new projects using the breadth and depth of the expertise gathered in ISO/TC 212; focus on horizontal standards; address topics that are generally applicable to all IVD devices; and, limit the activities of ISO/TC 212 to a level that corresponds to the resources that are available (time and funds of the delegates).

- Assign high preference to standards for developed technologies; assign high preference to performance-oriented standards; take the potential cost of implementation of a standard into consideration; and, solicit New Work Item ideas only according to perceived needs, which should be fully explained and supported by evidence.

- Globalize regional standards that have a global impact.

ISO/TC 212

ISO/TC 212:

- Technical Committee on Laboratory Medicine and *in vitro* diagnostic Systems

- participating countries: 32
  observer countries: 16

- secretariat: CLSI (former NCCLS) on behalf of ANSI

ISO/TC 212

Scope of ISO/TC 212:

Standardization and guidance in the field of laboratory medicine and in vitro diagnostic test systems. This includes, for example, quality management, pre- and post-analytical procedures, analytical performance, laboratory safety, reference systems and quality assurance.

Excluded:

- generic quality management standards dealt with by ISO / TC 176;
- quality management standards for medical devices dealt with by ISO / TC 210;
- reference materials guidelines dealt with by the ISO Committee on Reference Materials (REMCO);
- conformity assessment guidelines dealt with by the ISO Committee on Conformity assessment (CASCO).

ISO/TC 212

Relevant Standards in ISO/TC 212 (1):

- ISO 15193:2002
  In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Presentation of reference measurement procedures
- ISO 15194:2002
  In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Description of reference materials
- ISO 15195:2003
  Laboratory medicine – Requirements for reference measurement laboratories

ISO/TC 212

Relevant Standards in ISO/TC 212 (2):

- ISO 17511:2003
  In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and control materials
- ISO 18153:2003
  In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values for catalytic concentration of enzymes assigned calibrators and control materials
- ISO/WD 25680
  Laboratory Medicine – Estimation and reporting of measurement uncertainty of routine values

ISO/TC 212

Other ISO/TC 212 Standards of Interest:

- ISO 15189:2003
  Medical laboratories – Particular requirements for quality and competence
- ISO 15190:2003
  Medical laboratories – Requirements for safety
- ISO/TR 22869:2005
  Medical laboratories – Guidance on laboratory implementation of ISO 15189: 2003
- Project under consideration:
  Medical Laboratories – Genetic testing – Specific requirements for quality and competence

Reference Materials for Genetic Testing
-
ISO Standardization

Summary

- ISO standards are documents, not reference materials
- ISO standards should be performance rather than prescriptive standards
- ISO standards tend to be high level (horizontal) rather than single product related (vertical) standards
- Scope and structure of ISO/TC 212 qualify it to develop standards for reference materials
- Corresponding ISO/TC 212 standards have been implemented

Basics of ISO Standardisation Definitions

Genetic Testing:

Analysis performed on human DNA, RNA, genes, and/or chromosomes to detect heritable or acquired genotypes, mutations, phenotypes, or karyotypes that cause or are likely to cause a specific disease or condition. A genetic test also is the analysis of human proteins and certain metabolites, which are predominantly used to detect heritable or acquired genotypes, mutations, or phenotypes.

NOTE: The purposes of these genetic tests include predicting risks of disease, screening of newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations. (taken from a private communication from Joe Boone, CDC, 2005)

Basics of ISO Standardisation Definitions

Reference Material:

Material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of apparatus, the assessment of a measurement method, or foe assessing values to materials.

NOTE: A reference material may be in the form of a pure or mixed gas, liquid or solid. Examples are water for the calibration of viscometers, sapphire as a heat-capacity calibrant in calorimetry, and solutions used for calibration in chemical analysis. (International Vocabulary of Basic and General Terms in Metrology, ISO, 1993)